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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/693,558	10/20/2000	Elfi Biedermann	25846-0003	7777

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EXAMINER
SPIVACK, PHYLLIS G

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/693,558	Applicant(s) Biedermann et al.
	Examiner Phyllis G. Spivack	Art Unit 1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 6, 2003*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *32-52* is/are pending in the application.

4a) Of the above, claim(s) *41-49, 51, and 52* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *32-40 and 50* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 12
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Applicants' Response to the Restriction Requirement filed February 6, 2003, Paper No. 14, is acknowledged. Applicants have elected with traverse Group I directed to methods for preventing, reducing or eliminating side effects or neutralizing the side effects of a cancerostatic or immunosuppressive agent comprising administering a compound having vitamin PP activity of formulae II, IIa, IIb, III, IIIa, IIIb, IIIc, IV, IVa, IVb, V, Va or Vb, wherein no additional heterocyclic ring systems or sugars are present.

The previous request for an Election of species in Paper No. 6, is withdrawn.

An Amendment filed October 10, 2002, Paper No. 11, is further acknowledged in which new claims 50-52 were presented, and the dependencies of various claims were changed.

With respect to the traversal, Applicants argue the compounds having vitamin PP activity of Group II are heterocyclyl ethers and of Group III are sugar ethers of formulae II, IIa and IIb. Further, Applicants urge the claims have unity of invention; claims 32 and 33 are linking claims having vitamin PP activity; the composition claims of Group V are linked to the method claims by their activity; there is no undue burden; and, the restriction requirement is improper.

Applicants' arguments have been given careful consideration but are not persuasive. The Restriction Requirement as set forth is deemed proper for the reasons to follow and is maintained. Further, it is noted the request for an election of species was linked to the election of Group V only.

A plethora of compounds are encompassed both in the definitions of "a compound having vitamin PP activity" and of the R^{25} term of formulae IV, IVa and IVb in claim 33. The search required for one method, with a vitamin PP compound having various heterocyclic moieties, would vary from a vitamin PP compound that is a sugar. Distinctness of the methods is further evidenced by the different classification of the methods based on the different vitamin PP compounds. As to the burden of the search, classification is merely one indication of the burdensome nature of the search. The literature search of the large number of possible vitamin PP compounds claimed herein is not co-extensive and is a major factor in determining search burden. Where a sugar moiety or a particular heterocyclic groups is present in formulae IV, IVa and IVb, unity of invention is absent. These groups determine classification and present distinct functional moieties.

In no claim are the compounds disclosed in claim 38 administered as part of methods for preventing, reducing or eliminating side effects or neutralizing the side effects of cancerostatic or immunosuppressive agents. The assertion that claims 32 and 33 are linking claims is not seen as probative. The intended use of composition claims confers no patentable weight to the claims. The composition claims as set forth in Group V are not linked to the method claims.

The subject matter provisionally under consideration are those methods of use for preventing, reducing or eliminating side effects or neutralizing the side effects of a cancerostatic or immunosuppressive agent comprising administering a compound having vitamin PP activity of formulae II, IIa, IIb, III, IIIa, IIIb, IIIc, IV, IVa, IVb, V, Va or Vb, wherein no additional

heterocyclic ring systems or sugars are present, claims 32-40 and 50. Pharmaceutical compositions, claims 41-49, 51 and 52, and those methods of use comprising administering compounds with additional heterocyclic ring systems or sugars for R^{25} of formulae IV, IVa, or IVb, are withdrawn from consideration by the Examiner, 37 C FR 1.142(b), as being directed to non-elected inventions. Re-affirmation of the election of Group I is requested when Applicants respond to this Office Action.

An Information Disclosure Statement filed October 24, 2002, Paper No. 12, is further acknowledged and has been reviewed.

In the last Office Action claims 37 (claim 38 in the Office Action, an inadvertent typographical error) and 48 were objected to under 37 C FR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Following the amendment to claim 37, where the dependency has been changed to claim 32, the object is withdrawn. Claim 48 is now a non-elected claim.

Claims 32-49 were rejected in the last Office Action under judicially created doctrine as being drawn to an improper Markush group. A proper Markush group must share a substantial structural feature disclosed as being essential to the claimed utility. Lack of unity of invention has been found to exist since a common nucleus among the various compounds having vitamin PP activity, as tryptophan, or with possible heterocyclic groups or sugars, is absent. A prior art reference anticipating the claims under 35 U.S.C. 102 with respect to one species, such as tryptophan, would not render the same claims obvious under 35 U.S. C. 103 with respect to

another species, as a sugar. The members of the Markush groups possess widely different properties and are not considered functionally equivalent. The rejection is maintained with respect to claims 32-40 and 50.

Deletion of the non-elected subject matter would resolve the issue.

The rejection of claims 38-40 that were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention with respect to the recitation within the definitions of $R^{1(I)}$ through $R^{4(I)}$, $A^{(I)}$ and $D^{(I)}$ "functional group" is withdrawn following the amendment of Paper No. 11.

Claims 33-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The recitation for R^{27} in claim 33 "their ~~thio~~ analogs" lacks antecedent basis.

The recitation "anionic salts" at the end of claim 33 is confusing in that certain metal salts are toxic. The recitation "pharmaceutically acceptable salts" is suggested.

Claims 32-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The recitation within the definition of R^{25} in claim 33 "such that the alcohol

$R^{25}(OH)_a$" fails to define the invention properly. There is no alcohol depicted in formulae IV, IVa and IVb.

The recitation within the definition of R^{27} "in which a methylene group is optionally replaced by O, NH or N-alkyl" does not disclose the site at which the replacement occurs. Further, the terminal R^{27} cannot be O or NH.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 32-36 are rejected under 35 U.S.C. 102(a) as being anticipated by Budihardjo et al., Clinical Cancer Research.

Budihardjo teaches the therapeutic administration of the nicotinamide derivative, 6-aminonicotinamide, which can be metabolized in vivo to a compound with vitamin PP activity, as a modulator of the action of various antineoplastic treatments.

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 32-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Artemov, V.A., Vopr. Eksp. Klin. Immunol. (abstract).

Artemov teaches the administration of 5-hydroxy-6-methyl-3,4-pyridinemethanol, a compound of instant formula II, pyridoxine, to reduce the immunodepressive side effect of the cancerostatic agent 6-mercaptopurine.

No claim is allowed.

Any inquiry concerning this communication should be directed to Phyllis Spivack at telephone number 703-308-4703.

May 4, 2003

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER